REMARKS

Claims 1-16, 18-60 and 62-112 are pending in the application. Claims 1-8, 15, 16, 18, 30-37, 42-45, 47, 49, 50, 57-60, 62, 63, 75, 77, 79-85 and 89-91 have been rejected. Claims 9-14, 19-28, 38-41, 46, 48, 51-56, 64-71, 73, 76, 78, 86-88, and 92-112 have been withdrawn from consideration. Claims 1-8, 15, 16, 30, 31, 34, 35, 42, 45, 49, 50, 57-60, 62, 63, 75, 77, and 79 have been amended. Support for amendments can be found throughout the specification as originally filed, for example, on pages 21-22, paragraphs 75-78, and in the Examples. Applicants assert that no new matter has been introduced.

Claims 17, 18, 29, 43, 45, 47, 61, 72, 74, and 90 have been canceled without prejudice or disclaimer. In making this cancellation without prejudice, Applicants reserve all rights in these claims to file divisional and/or continuation patent applications.

Remarks to the Oath (Declaration)

In the Office Action, the Examiner alleged that the oath (declaration) is defective because the address of Himangi Jayakar was altered.

Applicants attach hereto a supplemental Declaration. Accordingly Applicants request withdrawal of the objection.

Double Patenting Rejections

In the Office Action, the Examiner provisionally rejected claims 45, 47, 49, 75, 77, 83, 84 and 89-91 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-20 of co-pending Application No. 10/327,673. Applicants disagree. Applicants request the Examiner holds such rejection in abeyance until such time as the Examiner indicates the claims are allowable.

Claim Objections

In the Office Action, the Examiner objected to claims 5, 34, 59 and 81 because of alleged informalities. The Examiner alleged that there is only one nuclear localization signal (NLS) that is to be deleted or mutated in the M protein. Claims 5 and 34 have been amended in order to cure these informalities. Claims 59 and 81 have been cancelled, rendering the objection moot. Accordingly, Applicants request withdrawal of the objection.

CLAIM REJECTIONS

35 U.S.C. § 112 Rejections

Applicants thank the Examiner for noting that the specification is enabling for recombinant VSV M protein with an alanine to methionine substitution at position 33 or 51 or a serine for glycine substitution at position 226 of the protein and for a deletion of amino acids 440-449 in VSV glycoprotein.

The Examiner rejected claims 1-8, 15, 16, 18, 30-37, 43-45, 47, 77, and 79-82 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement for claims to a recombinant Rhabdovirus with a mutation within a region encoding the membrane-proximal ectodomain of a Rhabdoviral G protein or mutation in the matrix (M) protein. Applicants disagree.

Applicants submit that one skilled in the art would know how to make and use a recombinant non-cytopathic Rhabdovirus, such as Vesicular Stomatitis Virus (VSV) with a mutation in the matrix (M) protein, as claimed and described in the subject Application. The subject application describes substitution of amino acids 33, 51, 133 and 226, for example in paragraph 222, and deletion of the entire matrix coding sequences and other mutations that results in reduced expression of the matrix sequences (see for example, pages 21-22, paragraphs 75-78). Examples 1-4 and accompanying figures 2, 10 and 11 describe embodied mutations in the M protein resulting in infectious yet non-cytopathic virus. One skilled in the art would necessarily know how to make and use M protein mutated non-cytopathic Rhabdovirus as claimed.

Applicants further submit that one skilled in the art would know how to make and use a recombinant non-cytopathic Rhabdovirus, such as Vesicular Stomatitis Virus (VSV) with a mutation in the glycoprotein (G) protein, as claimed and described in the subject Application. The subject application describes specific amino acid substitutions, for example on pages 24-25, paragraphs 82-86. Examples 5-10 and accompanying figures 21-23, and 28-32 describe embodied mutations in the G protein resulting in infectious yet non-cytopathic virus. One skilled in the art would necessarily know how to make and use G protein-mutated, non-cytopathic Rhabdovirus as claimed. Accordingly, Applicants request withdrawal of the rejection.

35 U.S.C. § 102 Rejections

Applicants thank the Examiner for admitting that claims 1-5, 7, 8, 15-18, 30-34, 36, 37, 43 and 44 are novel in view of Bell *et al.* and claims 1-3, 7, 8, 15, 16, 18, 30, 32, 36, 37, 43 and 44 are novel in view of Conzelmann.

Claims 45, 47, 49, 50, 57, 58, 60, 62, 63, 75, 77, 83-85 and 89-91 are rejected under 35 U.S.C. § 102(e), as allegedly being anticipated by Bell *et al.* (2004/0170607). Applicants disagree. Applicants maintain that the claimed mutations are drawn to a G protein with a mutation in the membrane-proximal ectodomain of the G stem polypeptide, which spans amino acids 421-462 of the G protein (see for example, paragraphs 81-85, pages 23-24, and Examples 5-7 of the specification as originally filed), which results in a Rhabdovirus with decreased viral membrane fusion. The claims are directed to, *inter alia*, specific substitution mutations within this region, *inter alia*, at amino acid positions 457, 461 (SEQ ID NO: 8, 10, 12, 13 and 14), amino acid position 452 (SEQ ID NO: 6), amino acid position 458 (SEQ ID NO: 9) and/or amino acid positions 456 or 457 (SEQ ID NO: 14), and further emphasizes the importance of the region between F440 and N449, which includes the conserved FFGDTG motif, in viral membrane fusion, since deletion of this region completely abolished fusion activity (paragraph 81, page 23). Bell *et al.* describe numerous mutations throughout the VSV genome, but do not specifically describe the claimed substitution or deletion mutations, nor are the methods of use of such recombinant VSV described. Accordingly, Bell *et al.*, do not anticipate claims 45, 47, 49, 50, 57, 58, 60, 62, 63, 75, 77, 83-85 and 89-91. Further, Bell *et al.* do not describe the importance of the G stem nor do they delineate a particular region of the G protein as distinct from any other portion of the G protein in terms of structure or function. Therefore, Bell *et al.* do not describe or provide foundation for the specific mutations of the subject. Accordingly, Applicants request withdrawal of the rejection.

Claims 45, 47, 49, 50, 60, 62, 63, 75, 77, 83-35 and 89-91 are rejected under 35 U.S.C. § 102(b), as being anticipated by Conzelmann (US 6,033,886). Applicants disagree. The instant claims 45, 47, 49, 50, 60, 62, 63, 75, 77, 83-35 and 89-91 are drawn to a Rhabdovirus with a mutation of the **membrane-proximal ectodomain** of the G protein (amino acids 421-462 of the 511-amino acid G-protein), which results in a Rhabdovirus with decreased viral membrane fusion activity. In contrast, Conzelmann describes deletion of the last 46 amino acids of the G protein (i.e. amino acids 465 – 511) (Example 6, column 16, lines 7-8) corresponding to the G protein **cytoplasmic tail** (column 16, lines 18-20), or deletions of the entire G protein (Example 7, column 16), for producing non-infectious rabies virus. The

mutations described in Conzelman do not correspond to the claimed deletions or substitution mutations of the membrane-proximal ectodomain of the G protein, nor does Conzelmann describe the claimed uses of such sequences therefore. Accordingly, Conzelmann does not anticipate claims 45, 47, 49, 50, 60, 62, 63, 75, 77, 83-35 and 89-91. Further, Conzelmann neither describes nor provides a foundation for the importance of any specific portion of the G protein, and certainly not the membrane-proximal ectodomain of the G protein, for inhibiting infection in G protein-mutant rabies viruses. Conzelmann does not delineate a particular region of the G protein as distinct from any other portion of the G protein in terms of structure or function, nor does he describe the specific mutations of the subject application. Accordingly, Applicants request withdrawal of the rejection.

As noted in MPEP Section 821.04, upon indication of allowable claims, claims for process of making and/or using the product which depend from an allowable claim may be rejoined. Accordingly, Applicants request rejoinder of claims 9-14, 19-28, 38-41, 46, 48, 51-56, 64-71, 73, 76, 78, 86-88, and 92-112 upon indication of allowable claims..

In view of the foregoing amendments and remarks, the pending claims are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

Please charge any fees associated with this paper to deposit account No. 50-3355.

Respectfully submitted,

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